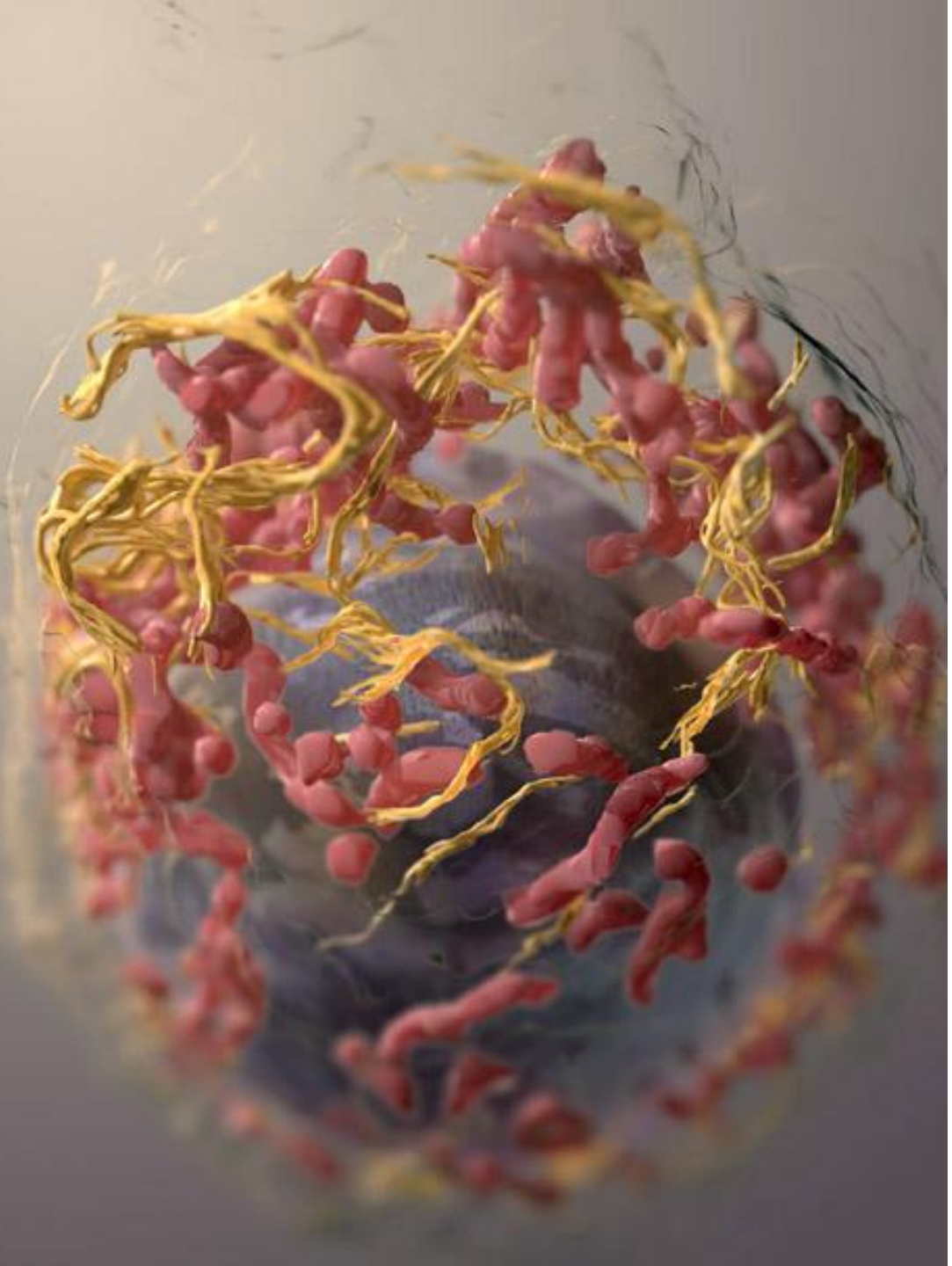


Cell Analysis Working Group

Jayne B. Morrow, PhD

National Institute of Standards and Technology

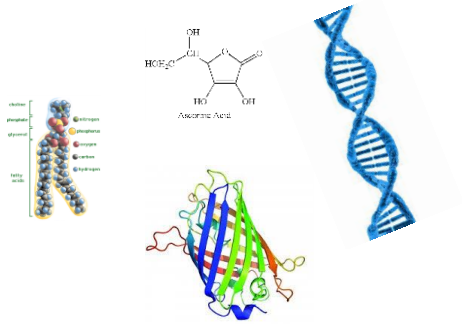
Our Charge

1) To carry out Key Comparisons and pilot studies, to critically evaluate and benchmark NMI/DI claimed competences for measurement services and capabilities including, but is not limited to the identification and quantification of cells and cell properties indicative of function as a result of emergent behavior in complex matrices and mixtures.

2) To identify and establish inter-laboratory work and pilot studies to enable global comparability of cell analytical measurement results through reference measurement systems of the highest possible metrological order with traceability to the SI, where appropriate and feasible, or to other internationally agreed units, in response to the demands of NMI customers.

Domains of Cell Analysis WG

Emergent behavior: novel *properties* that arise from a collection of constituents that do not themselves exhibit such properties.



Physical Components:
DNA, proteins, sugars, lipids

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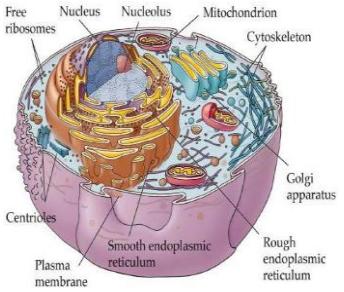


Biological system

- Cell analysis includes measurements of quantity of intact cells and cell properties indicative of function that are the result of emergent behavior.

- Relevant studies will include quantification of cell number or cell components *(e.g. cell surface receptors, in situ genes or proteins)*, and measures of biological response or function *(e.g. morphology, secretion of factor, expression rate of one or more genes)* in the context of cell emergent behavior. Work to develop measurements for cell and cell component identification will be coordinated with the other biological working groups.

Current and Near-Term Measurement Services

Reference Material Production

Eukaryotic Cell Systems

- Viable cell count 2D and 3D extracellular matrices (NPL, INRIM, LGC, NIBSC, KRISS)
- Concentration of blood cells in a blood matrix (NIBSC, VNIIIM, UME, LGC)
- Concentration of cell surface properties, CD4+, CD34+/CD45+ (NIST, VNIIIM, UME, LGC, NIBSC)

Prokaryotic Cell Systems

- Biodegradation potential (BAM)
- Pathogens in water (NIMC, NIMSA, IRMM)
- Pathogens in food (NIMC, ISP, IRMM)

Cell analogs

- Peptide or lipid micro-shells (NPL, NIBSC)
- Microspheres (NIST, NMIJ, NIMC)

Reference Data

Calibration and measurement services

- Flow cytometry – biomarker expression (NIST, INRIM)
- FACS – internal standards (shell, sphere) for cell counting (NPL)

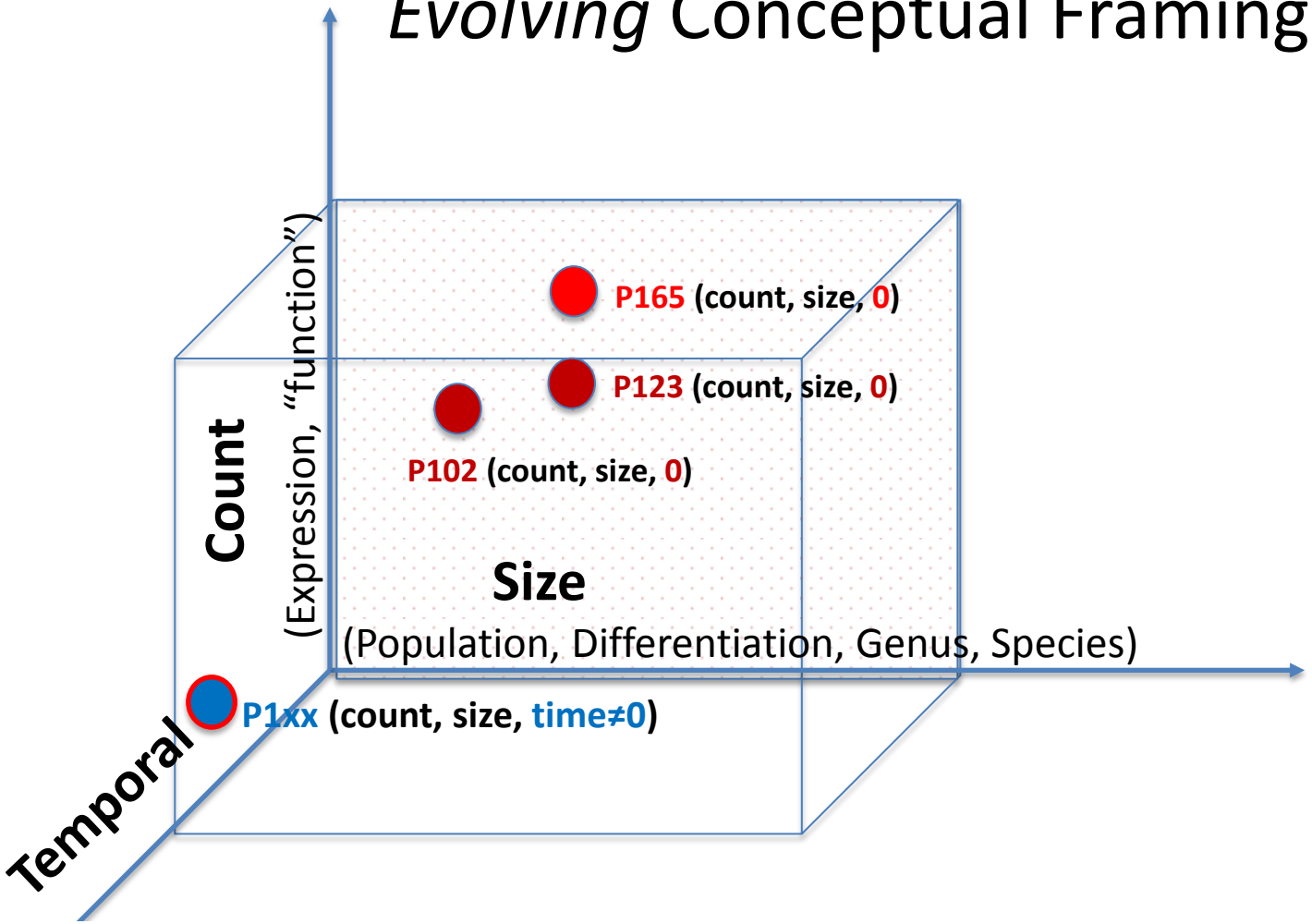
Reference value assignment

- Complete blood count (PTB, NIMC)
- Reference Value – adherent cell on 2D support (INRIM)
- Concentration of CD4+, CD34+/CD45+ (PTB)
- Antimicrobial susceptibility and biocidal properties (NPL, BAM)
- Cell viability measurements (NIMC, NPL)
- Cell count, yeast cell count (NIST)

Proficiency test organizer and regional comparability coordination

- Blood cell counting (PTB, NIMC)
- Pathogens in food (ISP, NIMC, NMIA)

Evolving Conceptual Framing



Pilot Study Proposals Anticipated September 2017

- Mammalian cell type, built on P123 (fixed cells on a substrate only substrate will change)
- Mammalian cell type, built on P165 (population dependent cell count by flow cytometry)
- Microbial cell type, built on plate count study only will determine method with traceability

extras

Measurement Capability Development

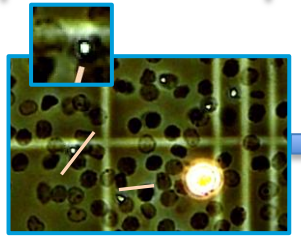
Sample collection

Sample storage and transportation

Reagents/Consumables

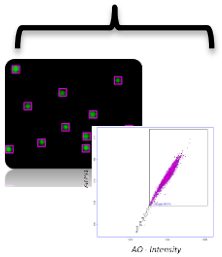
Sample preparation

Calibration and Instrument performance



Data collection

Calibration via known standards



Data analysis

- **Well characterized materials, Certified Reference materials, reference methods / protocols**
- **Documentary Standards**

Laboratories supported by current:

- **Quality Management System**
- **Conformity assessment**
- **Peer Review**

Our Scope

- Cell analysis will include measurements of composition or function of cells that are the result of emergent behavior.

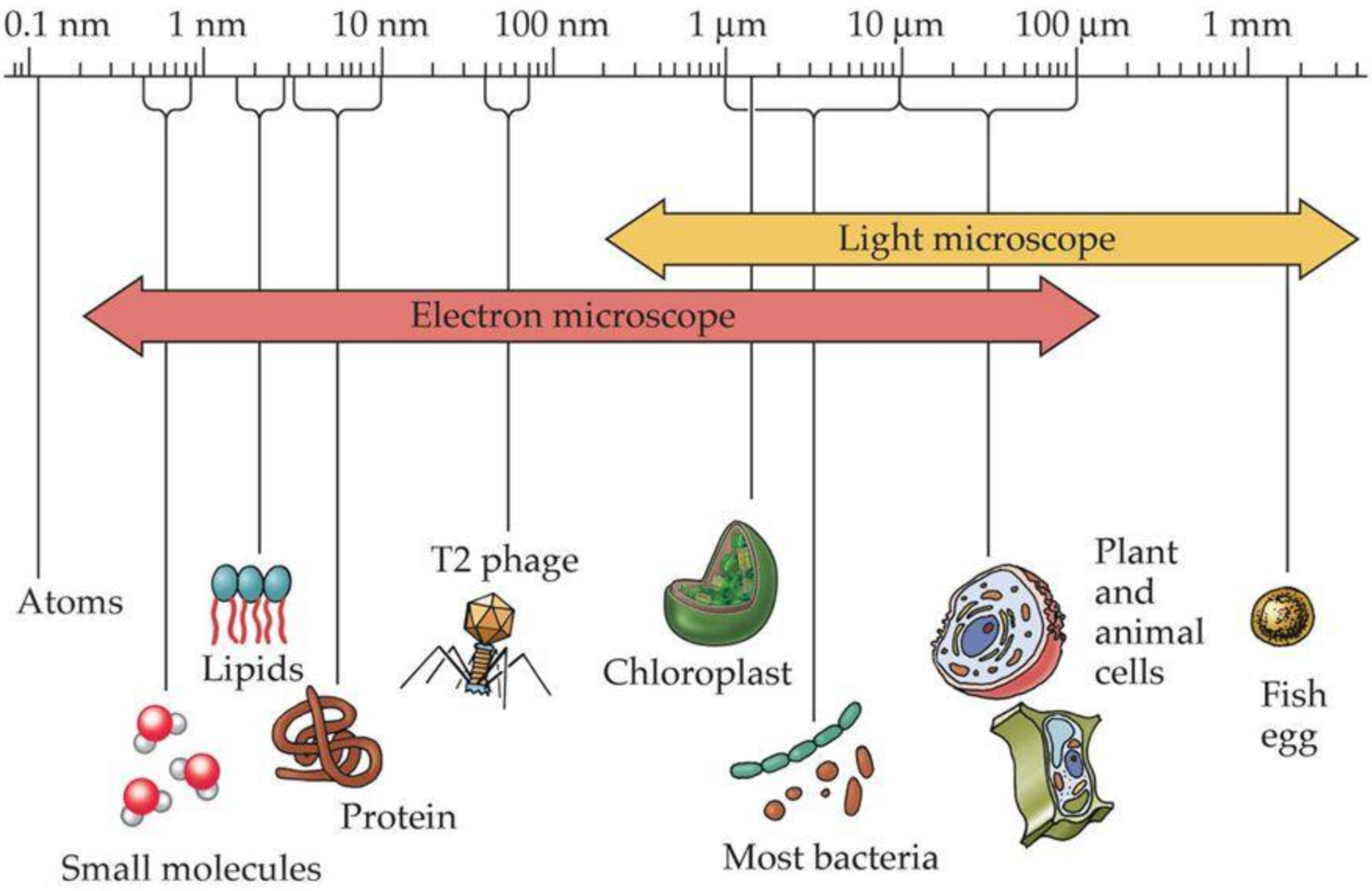
- Relevant measurements include identification and quantification of cell number or cell components *(e.g. cell surface receptors, in situ genes or proteins)*, and measures of biological response or function *(e.g. morphology, secretion of factor, expression rate of one or more genes)* in the context of emergent cell behavior.

- Measurements of genetics, genomics, transcriptomics, metabolomics, proteomics, etc. may be required to achieve measurement of the emergent behavior, and could be undertaken in collaboration with other WGs.

- Define the measurand carefully using validated methods resulting in metrological traceability that is also relevant or translatable to end-user application.

[Original: The measurand may not be easily defined. Validating the relevance of the measurand is critical to end-user application.]

Figure 4.2 *The Scale of Life*

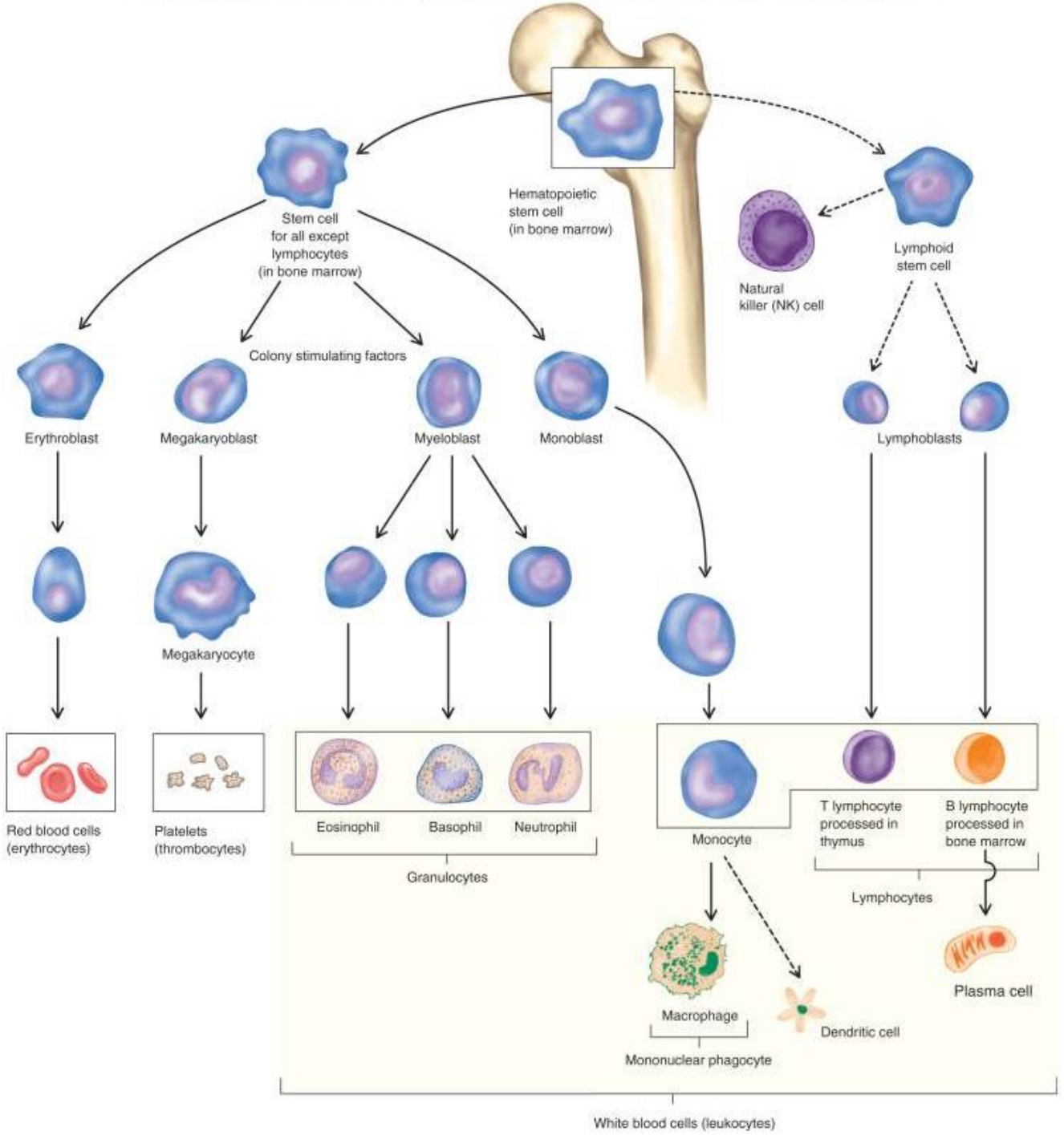


LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 4.2 The Scale of Life (Part 1)


Coccus
Rod, or bacillus
Curved forms: Spirillum/Spirochete
Diplococci (cocci in pairs)
Neisseriae (coffee-bean shape in pairs)
Coccobacilli
Vibrios (curved rods)
Tetrads (cocci in packets of 4)
Sarcinae (cocci in packets of 8,16, 32 cells)
Mycobacteria
Granules
Corynebacteria (palisades arrangement)
Spirilla
Streptococci (cocci in chains)
Micrococci and staphylo-cocci (large cocci in irregular clusters)
Spores
Spore-forming rods
Streptomycetes (moldlike, filamentous bacteria)
Spirochetes

RED BLOOD CELL MORPHOLOGY

Size variation	Hemoglobin distribution	Shape variation		Inclusions	Red cell distribution
Normal	Hypochromia	Target cell	Acanthocyte	Pappenheimer bodies (siderotic granules)	Agglutination
Microcyte	1+	Spherocyte	Helmet cell (fragmented cell)	Cabot's ring	
Macrocyte	2+	Ovalocyte	Schistocyte (fragmented cell)	Basophilic stippling (coarse)	Rouleaux
Oval macrocyte	3+	Stomatocyte	Tear drop	Howell-Jolly	
Hypochromic macrocyte	4+	Sickle cell	Burr cell	**Crystal formation**	
	Polychromasia (Reticulocyte)			HbSC HbC	


Hematopoietic stem cell (in bone marrow)
Stem cell for all except lymphocytes (in bone marrow)
Natural killer (NK) cell
Lymphoid stem cell
Colony stimulating factors
Erythroblast
Megakaryoblast
Myeloblast
Monoblast
Lymphoblasts
Megakaryocyte
Red blood cells (erythrocytes)
Platelets (thrombocytes)
Eosinophil
Basophil
Neutrophil
Granulocytes
Monocyte
T lymphocyte processed in thymus
B lymphocyte processed in bone marrow
Lymphocytes
Plasma cell
Macrophage
Dendritic cell
Mononuclear phagocyte
White blood cells (leukocytes)